DAC
JFW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Donald R. Huffman, et al.	**Examiner:**	S. Hendrickson
Serial No.:	07/580,246	**Art Unit:**	1754
Filed:	September 10, 1990	**Docket:**	7913Z
For:	FORM OF CARBON	**Dated:**	August 2, 2005

Confirmation No.: 5441

Mail Stop Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION UNDER 37 C.F.R. §§ 1.181/1.182 or 1.183

Sir:

I. INTRODUCTION

The above-identified application is on Appeal. The Appellants filed an Appeal Brief based upon the issues that were raised in the Final Rejection. The Examiner issued an Examiner's Answer.

However, the Examiner's Answer raised a new rationale in support of the rejection under 35 USC § 101. This issue was never raised in the Final Rejection. However, the Examiner's Answer did not designate this as a new ground of rejection, thereby not permitting Appellants to

---

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mailstop Petitions, Commissioner for Patents, Box 1450, Alexandria, VA 22313-1450.

Dated: August 2, 2005

Mark J. Cohen
Mark J. Cohen

08/08/2005 EAREGAY1 00000022 07580246
01 FC:1464 130.00 OP

option for reopening prosecution or to file an Appeal Brief, pursuant to 37 CFR § 41.39. Appellants respectfully Petition that the USPTO designate this rationale in support of the rejection as a new ground of rejection.

II. STATEMENT OF FACTS AND ARGUMENTS

A final Office Action dated October 7, 2003 rejected various claims under 35 USC. § 101 (see Exhibit 1). In its rejections, it referred to the rejections, comments and argument that were made in the rejection of November 30, 1993. A copy of the rejection of November 30, 1993 is attached hereto as Exhibit 2. The rationale provided in support of the rejection under 35 USC § 101 is described on pages 6 and 7 of Exhibit 2. It cites the article by Buseck et al. in Science, 257, 215-217 (1992), ("Buseck et al"), a copy of which is attached hereto as Exhibit 3. The Buseck article attached as Exhibit 3 makes allegations that C_{60} and C_{70} are found in fracture-filling films in shungite. It discusses that the fullerenes are present in minute amounts in shungite. A review of the article clearly establishes that there is no teaching or disclosure therein relating to sooty products or that macroscopic amounts of fullerenes are made by wood-fueled fires. Further, the Office Action of November 30, 1993 never raised any comment about macroscopic amounts of fullerenes found in wood-fueled fires.

However, with respect to the 101 rejection, the Examiner's Answer attached as Exhibit 4 states the following:

> Concerning the 101 rejection, it stands to reason that a macroscopic amount of fullerenes are made by a wood – fueled fire, given that flames particularly from aromatics are sooty and are black with particulates. Given what is argued by appellant throughout, especially at Brief, pg. 31, visible is equated with macroscopic.
>
> Id., See Page 4.

This is a new rationale in support of the rejection under 35 USC §101. This rationale was never presented in the Final Rejection. This issue was not described in Buseck et al, because Buseck et al never discussed wood- fueled fires, let alone the allegation that macroscopic amounts of fullerenes are made by wood- fueled fires. Moreover, the Final Office Action dated November 30, 2003 never made such an allegation. Moreover, based on the teachings in Buseck et al or in the Final rejection, there was no way for appellants to foresee this new ground of rejection.

In order to fully respond to the rejection, Appellants would like to utilize the article by Malhotra, et al. in J. Phy. Chem., 4599-4601 (1991) ("Malhotra, et al."), attached as Exhibit 5. Although this article was made of record in the underlying application in a Response dated March 1, 1993, it was not made of record as evidence to be considered by the Board of Patent Appeals and Interferences ("Board"), since it was not raised in the Final Rejection and was not relevant to the issues, as characterized in the Final Rejection.

If the USPTO designated this as a new ground of rejection, pursuant to 37 CFR §41.37, Appellants can exercise one of two options, either reopen prosecution and submit evidence to refute the rejection or maintain an Appeal and file a Reply Brief.

However, by not designating this as a new ground of rejection, Appellants can only file a Reply Brief in order to avoid dismissal of the Appeal. Moreover, according to 37 C.F.R. §§ 41.37 and 41.41, a Reply Brief cannot include new evidence, which Appellants interpret as meaning that a Reply Brief cannot present evidence that is not made of record on appeal. According to 37 CFR §41.41, a Reply Brief that is not in compliance with the rules will not be considered.

Appellants are thus prejudiced and deprived of an opportunity in filing a full Response to this new ground of rejection. Thus, through no fault of their own, Appellants in this Appeal cannot fully address the new ground of rejection. Moreover, Appellants cannot file the present application as an RCE inasmuch as this application was filed in 1991, and any patent issuing therefrom would only have approximately a six year term. Further, since it is an old application, no additional term can be added to the term of any patent issuing therefrom for the time it takes on appeal, as is the case of applications filed after June 8, 1995. Thus, the new ground of rejection which is not designated as such in the Examiner's Answer has the effect of either preventing Appellants an opportunity to be heard on appeal regarding the issues raised or unconstitutionally deprives Appellants of its intellectual property rights by forcing Appellants to refile the application to address this issue, thereby unconstitutionally depriving Appellants of its potential enjoyment of the full term of any patent issuing on this application.

Appellants thereby respectfully petition the USPTO to designate the rejection as a new ground of rejection so as to give Appellant an opportunity to put all of its evidence regarding this rejection on record and to address this new issue raised for the first time in the Examiner's Answer.

Alternatively, Appellants respectfully petition under 37 CFR §1.182 a clarification of the regulations pursuant to 37 CFR §41 et seq. It is apparent that this situation is not specifically addressed in the regulations. Nevertheless, the present circumstances creates a hardship to Appellants if the USPTO can raise new rationales for a rejection and the Appellants do not have an opportunity to present new evidence on appeal and to address the new issues presented by the USPTO. Accordingly, Appellants respectfully petition the USPTO to allow Appellants, in

situations such as these where a new rationale in support of a rejection is not designated as a new ground of rejection, to have the right to exercise the options described in 37 CFR §41.39.

Alternatively, pursuant to 37 CFR §1.183, Appellants request the suspension of the rules. As indicated hereinabove, there is no mechanism in place that would permit Appellants to make Malhotra et al. of record in this appeal under the present circumstances. Justice requires that Appellants be afforded an opportunity to fully address the new rationale presented in the Examiner's Answer and to make Malhotra of record. If Malhotra et al. can be made of record in this appeal, the Appellants are given an opportunity to be heard on this issue and are thus given the opportunity to traverse the new ground of rejection. Thus, alternatively, Appellants respectfully request that the requirement that no new evidence be presented in the appeal be suspended in this case and Appellants be permitted to make Malhotra et al. of record in this appeal.

It is respectfully requested that the Petition be granted for the reasons given herein.

The fee of $130.00 pursuant to 37 CFR §§ 1.181-1.183 is enclosed herewith. However, if additional fees are associated with the filing of this paper, the Commissioner is authorized to charge Deposit Account No. 19-1013. A duplicate copy of this Petition is enclosed.

Respectfully submitted,

Mark J. Cohen

Mark J. Cohen
Registration No. 32,211

Scully, Scott, Murphy & Presser
400 Garden City Plaza, Suite 300
Garden City, NY 11530
Telephone: (516) 742-4343
MJC:kd:cm:ae

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
07/580,246	09/10/1990	DONALD R. HUFFMAN	7913Z	5441

7590 10/07/2003

SCULLY, SCOTT, MURPHY & PRESSER
400 GARDEN CITY PLAZA
GARDEN CITY, NY 11530

EXAMINER	
HENDRICKSON, STUART L	
ART UNIT	**PAPER NUMBER**
1754	

49

DATE MAILED: 10/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No. 09/580,246	Applicant(s) Wukusick
Office Action Summary	Examiner Hendrickson	Group Art Unit 1754

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

☒ Responsive to communication(s) filed on 7/11/02.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 45-51, 53-75, 77, 80, 81, 83-86, 88-90, 92-107, 109-180 is/are pending in the application.

Of the above claim(s) ____ is/are withdrawn from consideration.

☒ Claim(s) 85, 90, 94, 95 is/are allowed.

☒ Claim(s) 45-51, 53-75, 77, 80, 81, 83, 84, 86, 88, 89, 92, 93, 96-107, 109-180 is/are rejected.

☐ Claim(s) ____ is/are objected to.

☐ Claim(s) ____ are subject to restriction or election requirement

Application Papers

☐ The proposed drawing correction, filed on ____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on ____ is/are objected to by the Examiner

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)–(d)

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119 (a)–(d).

☐ All ☐ Some* ☐ None of the:

☐ Certified copies of the priority documents have been received.

☐ Certified copies of the priority documents have been received in Application No. ____.

☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a))

*Certified copies not received: ____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO–1449, Paper No(s). ____

☐ Interview Summary, PTO–413

☐ Notice of Reference(s) Cited, PTO–892

☐ Notice of Informal Patent Application, PTO–152

☐ Notice of Draftsperson's Patent Drawing Review, PTO–948

☐ Other ____

Office Action Summary

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejections, comments and arguments made in the withdrawn rejection of 11/30/93 are hereby repeated, and they are incorporated herein by reference. To summarize, the rejections are:

- objection to specification for 'macroscopic quantities/amount'.
- '112 first paragraph for 'macroscopic quantities/amount', applied to claims 53-72, 86, 96-107, 111-152, 154-180.
- '112 second paragraph for 2 cases of indefinite language, applied to claims 97-101, 109, 110, 115-118, 120, 121, 133-140, 156, 158-161, 171-180.
- '112 fourth paragraph, applied to claims 133, 134, 138, 161.
- '101 as being naturally occurring, applied to claims 45-51, 53-75, 77, 80, 81, 83, 86, 88, 92, 93, 96-107, 109-180.
- '102/103 in view of Kroto/Curl, applied to claims 45-51, 53-75, 77, 80, 81, 83, 84, 86, 88, 89, 92, 93, 96-107, 109-180.

The rejection over Kratschmer is withdrawn.

Applicant's arguments filed 7/17/02 have been fully considered but they are not persuasive. Concerning the term 'macroscopic' this issue has been decided in other proceedings. As no new matter in the specification has been added by this amendment, the determination of what is present therein remains the same as before. The arguments appear to be repeats of those made earlier; that a solution is colored does not imply that a macroscopic solid is present. The argument on pg. 16 is conclusionary, as it presupposes that macroscopic amounts of solid were deemed to have been prepared previously with different sizes of graphite, but this has not been accepted.

Concerning the recognition by others that mcroscopic amounts were made, it is true that this term has long been applied to the original process. See

Seshadri et al. Tetrahedron Letters vol. 33 (no. Unknown) pg. 2069 1992.

Bethune et al. Chem. Phys. Lett. Vol. 179 no. 1,2 pg. 181 12 April 1992.

Saito et al. Chem. Phys. Lett. Vol. 204 no. 3,4 pg. 277 19 March 1993.

It is not known what their criteria were.

The 4th paragraph rejection is maintained, as it is not agreed that a minute amount of a colored solution represents a macroscopic amount, even though the rejected claims recite a larer amount than this. Concerning Kroto/Curl, thereis insufficient data to determine how much C60 is need to be a 'solid' or a 'crystal'; the implication that this is an amount which is greater than what was just argued as constituting a 'macroscopic amount' is not accepted as it is not logical.

The Declarations are noted. The Declaration of Loutfy concerning the experiments is speculative. Concerning macroscopic, it repeats earlier arguments. The Declaration of Moravsky was sufficient to overcome the Kratschmer rejection. The other Declarations recited are taken to be references to old Declarations, no other new Declarations were found. It is not necessary to resubmit Declaration which repeat statements made in earlier Declarations, and given the amount of time since the original filing, only experiment Declarations should be filed, as conversations and observations made in 1990 may be misremembered or incomplete.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to examiner Hendrickson at telephone number (703) 308-2539.

Stuart Hendrickson
Primary examiner Art Unit 1754

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/580,246	09/10/90	HUFFMAN	D 79137

EXAMINER
KALINCHAK, S

11M1/1130

SCULLY, SCOTT, MURPHY & PRESSER
400 GARDEN CITY PLAZA
GARDEN CITY, NY 11530

ART UNIT	PAPER NUMBER
1103	

DATE MAILED: 11/30/93

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 3/4/93 ☑ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ ____________

Part II SUMMARY OF ACTION

1. ☑ Claims 45-77, 79-180 are pending in the application.

Of the above, claims ____________ are withdrawn from consideration.

2. ☑ Claims 1-44, 78 have been cancelled.
3. ☑ Claims 85, 90, 94, 95 are allowed.
4. ☑ Claims 45-77, 79-84, 86-89, 91-93, 96-180 are rejected.
5. ☐ Claims ____________ are objected to.
6. ☐ Claims ____________ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on ____________. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on ____________ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on ____________, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. ____________; filed on ____________
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. been received.

I. **Rejections**

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed.

Support is not found for the new term, "macroscopic quantities" that has been added to claims 86, 96, 102 - 108, 111 - 114, 119, 141, 162, and 165 - 168. Applicants rely on various portions of the disclosure in alleging support exists. Specifically, Applicants refer to the disclosure of "recoverable amounts," the x-ray diffraction of "crystals," the IR spectrum obtained from a 2 micron thick coating, and the fact that a specific color was observed. However, none of these disclosures require the presence of "macroscopic quantities." Microscopic quantities or less can be recovered, crystals are very often

microscopic as opposed to macroscopic, x-ray and IR data can be obtained from less than macroscopic quantities, and color can be observed under a microscope. As to the 2 micron thick coating, there is no indication of record that such a small coating, i.e. 2 ten-thousandths of a centimeter, can in fact be seen.

Moreover, insertion of "macroscopic amounts" into the claims is not supported because the new phrase represents a broadening of the scope of the original disclosure. To illustrate, the literal language of the original disclosure supports the production of fullerene in quantities sufficient to produce coatings that are 2 microns thick. However, the new term "macroscopic amounts" extends the disclosure of the amount of fullerenes produced from this minimal amount to amounts far in excess, e.g. one ton of fullerenes. There is no disclosure supporting or describing larger quantities of fullerenes as embraced by the term "macroscopic amounts." Applicants have not specifically pointed out where support exists for the production of macroscopic quantities of C_{70}. The specification states that the product is only 2% C_{70}. If support for the production of macroscopic quantities of fullerenes in general is tenuous, then the question of whether macroscopic quantities of C_{70} is supported by the disclosure of only 2% is C_{70} is more in doubt.

The facts of the instant case are controlled by those of <u>In re Barker</u>, 194 USPQ 470 (CCPA 1977). In this case, the original

disclosure contained drawings that showed contemplation of an embodiment of making prefabricated panels of wooden shingles where the backing board had lengths of four or eight feet with a repetitive series of eight or sixteen shingles per backing board. Id. at 471, 474. This disclosure was held not to support or describe an amendment requiring the backing board to have a length at least as great as the aggregate width "of at least six shingles." Id. at 474. Accordingly, the court did not allow extension of the disclosure from a backing board long enough to hold eight or sixteen shingles to a backing board long enough to hold "at least six shingles."

Claims 86, 96 - 108, 111 - 152, and 154 - 180 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 97 - 101, 109 -110, 115 - 118, 120 - 121, 133 - 140, 156, 158 -161, 171 - 180 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) In claims 97 -101, 109 -110, 115 - 118, 120 - 121, 133 - 140, 158 -161, 171 - 180 the recitations of "amounts capable of . . . " being detected by various analytical instruments are indefinite. The lower limit of the quantities recited in the instant claims is unclear as detection limits of the recited

instruments are subject to change, and may vary from instrument to instrument. For example, the Examiner takes Official Notice that the detection limits of a single beam IR vary significantly from that of a Fourier Transform IR. The claims do not specify which type of instrument serves as the standard. Further, the detection limits of any instrument vary with the type of sampling method used. Again, the instant claims are silent as to which sampling methods have been used to define the lower limits of the claim. Accordingly, the claims are indefinite as one of ordinary skill in the art would be unable to determine the metes and bounds of the claims with the information provided.

b) In claim 156 the recited Markush group is indefinite as the species are not mutually exclusive. Ex parte Clark, 174 USPQ 40 (Bd. of Appeals 1971). Note that several species are repeated. Also, "crystallization" embraces fractional crystallization and "column chromatography" can be considered to be generic to HPLC. It also appears that "fractionally" should be changed to "fractional."

Claims 133 - 134, 138, and 161 are rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

These claims fail to limit the claims from which they depend requiring that macroscopic quantities be present. Note that a microphotograph may be taken of any substance, regardless of its

quantity or size. Assuming Applicants intend to recite a limitation that requires that the crystals somehow be microscopic in size or quantity, such a limitation would be indefinite as being inconsistent with the independent claims, expressly requiring "macroscopic quantities."

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 45-77, 79-83, 86-88, 91-93, and 96 - 180 (absent new matter) are rejected under 35 U.S.C. § 101 because the invention as claimed embraces products found in nature as shown by the Buseck et al. article. As set forth by the Commissioner of Patents and Trademarks, Official Gazette, 1077 O.G. 24 (1987):

> Products found in nature will not be considered to be patentable subject matter under 35 USC 101 and/or 102. An article of manufacture or composition of matter occurring in nature will not be considered patentable unless given a new form, quality, properties or combination not present in the original article existing in nature in accordance with existing law. See e.g. Funk Bros Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 76 USPQ 280 (1948); American Fruit Growers v. Brogdex, 283 U.S. 1, 8 USPQ 131 (1931); Ex parte Grayson, Si USPQ 413 (Bd. App. 1941).

This rejection will apply to claims 86, 96, 102 - 108, 111 - 114, 119, 141, 162, and 165 - 168 only if Applicants delete the term "macroscopic amounts" in the claims. If Applicants elect not to cancel the term "macroscopic amounts" from these claims for appeal, this rejection over the claims containing the new

term "macroscopic amounts" will be withdrawn.

Claims 45-77, 79-84, 86-89, 91-93, 96 - 180 (absent new matter) are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over the Kroto et al. article in Nature, Vol. 318, p. 162, November 14, 1985 with the Curl et al. article in Scientific American, October 1991 page 54 cited to show an inherent state of fact.

This rejection will apply to claims 86, 96, 102 - 108, 111 - 114, 119, 141, 162, and 165 - 168 only if Applicants delete the new matter, "macroscopic amounts" in the claims. If Applicants elect not to cancel the term "macroscopic amounts" from these claims for appeal, this rejection over the claims containing the new term "macroscopic amounts" will be withdrawn.

As discussed in the Nature article, Kroto et al. detected C_{60} and C_{70} fullerenes in soot produced by the laser evaporation of graphite. The C_{60} and C_{70} were detected or measured by means of time of flight mass spectrometry, and the amount of C_{60} and C_{70} molecules produced was on the order of tens of thousands (see the Curl et al. article in Scientific American, October 1991, pg. 54, third column). The Examiner notes that the detection method used by Kroto et al. detected the C_{60} and C_{70} in the vapor state, thereby anticipating the instant claims 82, 86, 87 and 91.

The instant claims 48-51, 75, 81, 83, 88 and 91-93 require

that the C_{60} or C_{70} be incorporated into a solid matrix. The disclosure of Kroto et al. inherently meets this requirement as solid particulate of free flowing soot is "formed" in the evaporation chamber. Given the well known stability of the fullerenes produced it is inherent that the fullerenes not directed to the mass spectrometer are inherently incorporated into the soot mixture, which is either amorphous or crystalline. Thus, the instant claims are anticipated in this respect. Also, the limitation that the product be formed and extended in at least one direction is noted. This is not seen to distinguish the instant product because the limitation reads on any particle that has a definite size. As to the "consisting essentially of" language of claims 45-47, the burden is on Applicants to show that the added component of the solid product of Kroto et al., i.e. soot, is contrary and inimical to the instant invention in terms of utility.

The instant claims 52, 73, 74, 76 and 79 are directly anticipated by the teaching of Kroto et al.. Note that immediately after the graphite is vaporized, the helium atmosphere in the apparatus of Kroto et al. contains a carbon product that comprises a mixture of C_{60} and C_{70}. Regarding the instant claims that define the properties of C_{60} and C_{70} fullerenes such as the mass spectra, infrared spectra, UV spectra, solubilities, sublimation temperatures and color, the Examiner

notes that these are all inherent properties of the C_{60} and C_{70} molecules produced and detected by Kroto et al. which have subsequently been confirmed in the art. It is also noted that the C_{60} and C_{70} of Kroto et al. is "formed" as the graphite is vaporized, thereby anticipating the instant claims 73 and 80. Regarding the instant limitations in claims 84 and 89 that the fullerenes be "substantially pure", as shown in Fig. 3 of the reference detection peaks for C_{60} and C_{70} are fully separated from other peaks thus indicating that the instrument has isolated the C_{60} and C_{70} form other substances in the matrix thus indicating that the two are "pure" or "substantially pure".

As to the instant product by process claims, for the reasons discussed above the C_{60} and C_{70} products of Kroto et al. are identical or only slightly different from that claimed. Thus, the instant product by process claims are rendered prima facie obvious by the teaching of Kroto et al. See MPEP 706.03(e).

Claims 45 - 77, 79 - 83, 87-88, 91-93, and 96 - 180 are rejected under 35 U.S.C. § 102(b) as being anticipated by the Kratschmer et al. article entitled "Spectroscopy of Matrix-Isolated Carbon Cluster Molecules Between 200 and 850 nm Wavelength."

The Kratschmer et al. article teaches a process of vaporizing graphite rods in an evacuated reactor under a slight

pressure of He gas (pages 815-816). Note that comparison of Figure 2 of the reference with the instant Figure 4 shows that the fullerenes inherently produced by the process were detected by UV. Because Applicants admit that macroscopic quantities are required to obtain UV data (see Response dated March 4, 1993, page 11, lines 13 - 15), the Kratschmer et al. product inherently contains macroscopic amounts of fullerenes.

II. Response to Applicants' Arguments

Applicant's arguments filed March 4, 1993 have been fully considered but they are not deemed to be persuasive.

In response to the rejection made under 35 U.S.C. 101 citing Buseck et al. to show that the subject matter as claimed occurs in nature, Applicants assert that the claimed invention takes on a new form than the natural material of Buseck et al. and is therefore patentable under section 101. From the arguments offered, this new form appears to lie in the quantity and purity of the fullerenes. However, there are no limitations in the rejected claims (other than the new term "macroscopic") to distinguish the quantity and purity of the claims from those described to occur in nature by the reference. It is noted that the fullerenes contained in the shungite rock are solid, as admitted by Applicants (see Response dated March 4, 1993, page 17, lines 22 -23). In short, Applicants' arguments are not persuasive because they are not commensurate in scope with the

rejected claims.

Applicants' citations of case law are not persuasive as the district court and 4th Circuit cases have not been adopted by the Federal Circuit and are therefore not controlling authority.

Regarding the rejection made under 35 U.S.C. 102(b) over the Kroto et al. article, Applicants contend that this reference is not enabling. However, Applicants' citation to United States v. Teletronics, Inc., 857 F.2d 778 (Fed. Cir. 1988), stating that the test of enablement is whether one of ordinary skill in the art could make the invention as claimed from the disclosure of the reference supports the fact that the Kroto et al. article is enabling. The Kroto et al. article gives a detailed description on how the fullerenes were made in quantities on the order of tens of thousands of molecules (see Figure 2). The claims rejected over this reference read on the quantities of fullerenes made by Kroto et al.. Accordingly, the Kroto et al. article enables one of ordinary skill in the art to make the instant product as claimed. Applicants apparently allege that the Kroto et al. article states that attempts to make the claimed fullerenes failed. No such statements have been found nor pointed out in the reference. The argument that the step of slurrying the soot produced by Kroto et al. with benzene did not produce a colored solution speaks to the quantity of fullerenes produced, and does not preclude the inherent production of trace

amounts of solid fullerenes in the soot as described in the rejection. Again, the rejected claims read on trace quantities of fullerenes.

At this point, the Examiner notes that the instant claims 85, 90, 94, and 95 are allowable over the prior art of record.

III. Additional Matters

As to the Information Disclosure Statement filed June 24, 1992, the references crossed out therein were not in compliance with 37 CFR 1.98(a)(2) as copies of these references were not received.

The Blau et al. article entitled "An Investigation of the Microfrictional Behavior of C_{60} Particle Layers on Aluminum" is cited as pertinent to lubricants.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Stephen Kalinchak at telephone number (703) 308-1093.

SGK
S. Kalinchak/rw
November 30, 1993

Michael Lewis
Supervisory Patent Examiner
Patent Examining Group 110

Fullerenes from the Geological Environment

Peter R. Buseck, Semeon J. Tsipursky, Robert Hettich

By means of high-resolution transmission electron microscopy, both C_{60} and C_{70} fullerenes have been found in a carbon-rich Precambrian rock from Russia. The fullerenes were confirmed by Fourier transform mass spectrometry with both laser desorption and thermal desorption/electron-capture methods to verify that the fullerenes were indeed present in the geological sample and were not generated by the laser ionization event. The mass spectra were measured under conditions sufficient to resolve the $^{13}C/^{12}C$ isotopic ratios for C_{60} and C_{70} and indicate that these ratios correspond to the normal range of isotopic values.

Fullerenes were discovered as an outgrowth of an investigation of carbon clusters that presumably occur in interstellar atmosphere (*1, 2*). Subsequent studies were made with the goal of locating them in meteorites (*3–6*), but the searches have been unsuccessful. In spite of the intensive research that has occurred since it became possible to make fullerenes in macroscopic quantities (*7, 8*), there are no confirmed occurrences of fullerenes formed in the natural environment. In the laboratory they have been synthesized by laser ablation (*9*), in carbon arcs (*7*), and by burning benzene (*10*). Their apparent absence is perhaps not surprising because they are synthesized at temperatures greater than occur in the natural environment outside of extreme conditions (lightning strikes, stellar interiors). Another constraining factor in natural environments is the effect that oxygen, nitrogen, and other non-inert gases have on inhibiting the growth of fullerenes.

Here we report an occurrence of fullerenes from the geological environment. We found them while examining high-resolution transmission electron microscopy (HRTEM) images of poorly graphitized material by noticing the similarity to images of synthetic fullerenes (*11*). We subsequently confirmed the presence of C_{60} and C_{70} by mass spectrometry. They occur within fracture-filling films in shungite, an usual carbonaceous rock found near the town of Shunga in Karelia, Russia.

Shungite has been the subject of intensive investigation for over a century (*12, 13*). It occurs in a metamorphosed carbon-rich rock within Precambrian sediments; the host formations are, according to Volkova and Bogdanova (*14*), seams of sedimentary origin. The overlying rocks consist of gray dolomitized sandstones and poorly sorted silts and clays, and the underlying rocks are not exposed. The shungite consists of masses containing up to 99% carbon. Diabase is interstratified with shungite-bearing rocks, and the shungite concentration increases with proximity to the diabase. Our sample comes from inclusions in the diabase.

Based on its optical characteristics, Firsova and Yakimenko (*15*) classified shungite into four groups. Our sample belongs to their shungite 1c group. Volkova and Bogdanova grouped it into five types, based largely on carbon content, mineral matter, and luster. Khavari-Khorasani and Murchison (*16*) simply divided it into "bright" and "dull" varieties based on its appearance in hand specimen; the former has a high luster and higher carbon content whereas the "dull" variety has a matte appearance. Our sample is of the bright variety.

The origin of shungite has been a continuing source of controversy ranging from organic (*14*) to volcanic (*17*). Firsova and Yakimenko (*15*) concluded that shungite formation was strongly affected by metamorphic processes. Volkova and Bogdanova (*14*) believe that it represents ancient coal beds within sediments, and that shungite is the most highly metamorphosed coal known; they point out that it has features typical of both humic and sapropelic coals and shows structures that they interpret as woody remains.

Compositionally, shungite represents coals of the meta-anthracite rank, characterized by low ash and sulfur contents, low volatile yields, and high carbon contents. Although Volkova and Bogdanova (*14*) describe organic features that they interpret as evidence of Precambrian life, the last sentence of their paper curiously raises the possibility that the shungite is not Precambrian in age. Schopf (*18*) believes shungite is "coaly" rather than a proper coal and that it is remobilized material formed by devolatilization of organic remains. If a coal, it would probably be best grouped with the anthraxolites, but it seems more likely that it has its origin from bitumens. Clearly, uncertainty exists regarding this unusual rock type.

There are several examples of Precambrian coals, of all which are of interest because of the potential information they provide about early forms of life (*19–22*). Tyler *et al.* (*19*) report the occurrence of thin, highly reflecting graphitic films in their Precambrian coal samples. It is intriguing to speculate that these veins may also contain fullerenes. We obtained a piece of the material collected by Tyler, but we have not observed any of the veinlets.

The samples we studied are pure black, have high reflectivity (resembling jet or obsidian), conchoidal fracture, and contain small, curling fractures that resemble narrow dessication cracks. The fractures are filled with carbonate. In some cases the fracture walls are coated with thin, dark, yellowish-brown films of carbon that have a submetallic luster. TEM study shows the films

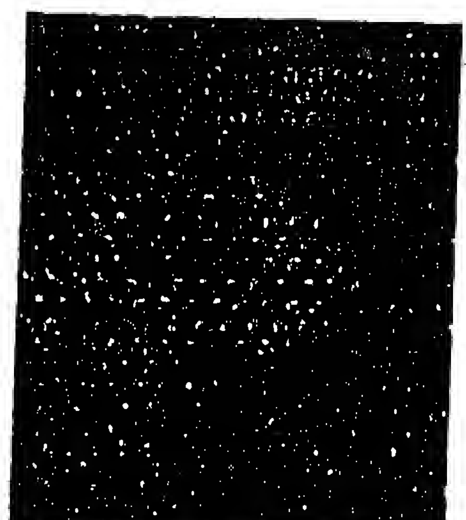

Fig. 1. (A) HRTEM image of fullerenes in a shungite sample. The rounded shapes are C_{60} and perhaps C_{70} molecules, arranged in a close-packed array. The inset shows a relatively well-packed array of molecules. (B) HRTEM image of synthetic fullerenes at the same magnification as the inset of (A) [S. Wang, Arizona State University]. The contrast between (A) and (B) differs slightly because of small differences in TEM operating conditions.

P. R. Buseck, Departments of Geology and Chemistry, Arizona State University, Tempe, AZ 85287.
S. J. Tsipursky, Department of Geology, Arizona State University, Tempe, AZ 85287.
R. Hettich, Analytical Chemistry Division, Oak Ridge National Laboratory, Oak Ridge, TN 37831.

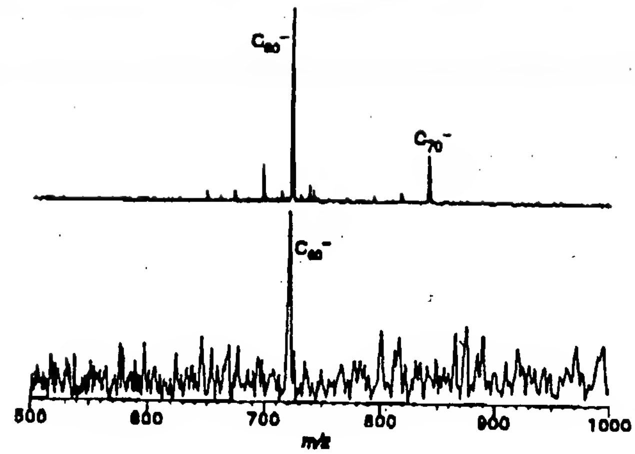

Fig. 2. Negative-ion FTMS spectrum of fullerenes from shungite. The laser-desorption spectrum (top) indicates the presence of C_{60} and C_{70} but no larger fullerenes. Thermal desorption measurements (bottom) verify the presence of significant amounts of indigenous C_{60} in this sample. The vertical scale represents relative abundances and is dimensionless.

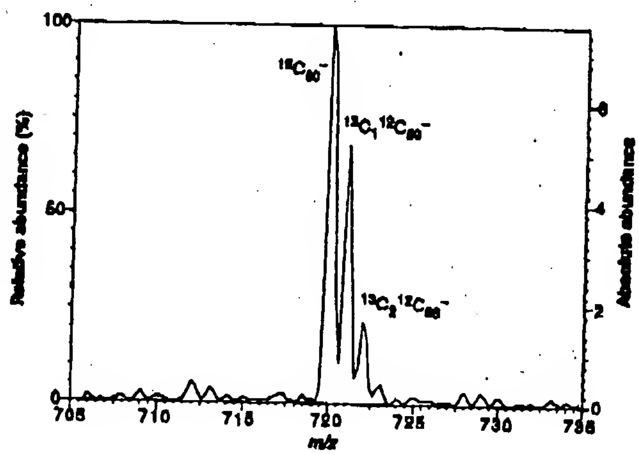

Fig. 3. High-resolution, laser-desorption FTMS spectrum showing the isotopic abundances of C_{60}. The isotope ratios are as follows: for m/z = 720, 100% (calculated) versus 100% (measured); for m/z = 721, 67% (calculated) versus 68% (measured); and for m/z = 722, 24% (calculated) versus 22% (measured).

consist of irregularly shaped particles 0.1 to 1 μm in diameter (*23*). Most are amorphous, but in some HRTEM images we observed features that we interpret as individual molecules and small regions of fullerenes. They are unevenly distributed and minor in abundance. In the images the fullerenes appear round (presumably roughly spherical in three dimensions), with white rims and black centers (Fig. 1A). They look almost identical to images of C_{60} molecules obtained by Wang and Buseck (*11*) (Fig. 1B).

A Fourier transform mass spectrum (FTMS) shows a strong peak at m/z 720, corresponding to C_{60}, and a weaker but still pronounced peak at m/z 840, which was identified to be C_{70}, (Fig. 2). Negative-ion mass spectra were obtained by laser desorption of samples that were ground and then transferred to glass slides (*24*). Laser-desorption FTMS (*25, 26*) is useful for the complete examination of fullerenes of types C_n, where n ≈ 50 to 400. The procedure generates both positive and negative ions, and either can be used to profile the fullerene content of a mixture. A potential problem for these studies is that under certain experimental conditions fullerenes can be generated by the laser process, thereby distorting the results. For example, under laser-ablation conditions (laser power densities greater than 10^8 W/cm^2), fullerenes can be generated from graphitic material (*27, 28*) and from coals (*29–33*). In contrast, low-energy laser desorption (power densities of 10^5 to 10^7 W/cm^2) is often used to profile the constituents of a sample and is less prone to generate species that were not originally present.

To avoid potentially generating fullerenes by high-energy laser ablation of graphitic materials, we used low laser energies and tested these on samples known to contain only graphitic material and no fullerenes. Mass spectra of these blanks were free of C_{60} and other fullerene peaks, verifying that under our experimental conditions we did not generate fullerenes during the laser desorption process. In addition, to check our laser-desorption results, the samples were thermally desorbed up to 350°C into the vacuum chamber, where they were ionized by low-energy electron capture. The ions were trapped, manipulated, and ultimately detected in the FTMS ion cell. While thermal-desorption, electron-capture experiments are dependent on fullerene volatility, it is possible to desorb C_{60} below 350°C (*34*), which was the highest temperature possible with our instrument and is at the threshold of desorbing C_{70}. The importance of the thermal desorption experiments is that there is no evidence that C_{60} can be generated from graphitic material under these experimental conditions. Thus, these experiments definitively established the presence of fullerenes in our samples, increasing our confidence in the initial HRTEM measurements (Fig. 1).

The ions from the shungite samples could be measured with adequate resolution to resolve the ^{13}C isotope contents for both C_{60} and C_{70}. Isotope ratios can be measured with 5% accuracies by carefully controlling the ion population and examining standard materials for isotope calibrations. The results indicate, within these error limits, normal isotopic abundances (Fig. 3).

Fullerenes are known to be highly stable with respect to temperature (*6*) and impact and static high pressure (*35, 36*). Their occurrence in what are probably Precambrian rocks suggests that they are also highly stable with respect to time, although we have no direct evidence that they did not form more recently as secondary products.

REFERENCES AND NOTES

1. H. W. Kroto *et al.*, *Nature* **318**, 162 (1985).
2. H. W. Kroto, *Science* **242**, 1139 (1988).
3. D. Heymann, *Lunar Planet. Sci. Conf.* XXII, 569 (1991).
4. M. S. De Vries *et al.*, *ibid.*, p. 315.
5. R. D. Ash, S. S. Russell, L. P. Wright, C. T. Pillinger, J. W. Arden, *ibid.*, p. 35.
6. I. Gilmour *et al.*, *ibid.*, p. 445.
7. W. Krätschmer *et al.*, *Nature* **347**, 354 (1990).
8. W. Kratschmer, K. Fostiropoulos, D. R. Huffman, *Chem. Phys. Lett.* **170**, 167 (1990).
9. E. A. Rohlfing, D. M. Cox, A. Caldor, *J. Chem. Phys.* **81**, 3322 (1984).
10. J. B. Howard, J. T. McKinnon, Y. Makarovsky, A. L. Lafleur, M. E. Johnson, *Nature* **352**, 139 (1991).
11. S. Wang and P. R. Buseck, *Chem. Phys. Lett.* **182**, 1 (1991).
12. A. A. Inostrantsev, *Gornil Journal* **2**, 314 (1879).
13. ———, *ibid.*, p. 35 (1886).
14. I. V. Volkova and M. V. Bogdanova, *Intl. J. Coal Geol.* **6**, 369 (1986).
15. S. O. Firsova and E. P. Yakimenko, *Lith. Min. Res.* **1**, 88 (1985).
16. C. Khavari-Khorasani and D. G. Murchison, *Chemical Geol.* **26**, 165 (1979).
17. V. A. Sokolov, *Shungity Karelii i puti ikh kompleknogo ispolzovanija* (Karelija, Petrozavodsk, 1975).
18. J. W. Schopf, private communication.
19. S. A. Tyler, E. S. Barghoorn, L. P. Barret, *Bull. Geol. Soc. Am.* **68**, 1293 (1957).
20. K. Rankama, *ibid.* **59**, 389 (1948).
21. L. E. Sterenberg, *Doklady AN USSR* **148**, 888 (1963).
22. M. Schidlowski, *Umschau in Wissenschaft und Technik* **68**, 566 (1968).
23. Specimens were prepared by hand-picking films from rock chips, first for TEM study and then, some weeks later after the TEM results were obtained, for mass spectrometry. Following initial measurements on a Finnegan MAT312 magnetic sector mass spectrometer at Arizona State University, additional sample fragments were hand-picked and sent to Oak Ridge for Fourier trans-

form mass spectrometry. For the TEM study, we used a JEOL JEM-4000EX transmission electron microscope with a top-entry, double-tilting sample holder (±15° tilt), a structure resolution limit of 1.7 Å, and a spherical aberration coefficient (Cs) of 1.0 mm. A 40-μm objective aperture and a 150-μm condenser aperture were used for high-resolution TEM.

24. Fourier transform mass spectra (FTMS) were obtained using an Extrel FTMS-2000 instrument. Fullerene ions were generated by either laser desorption (using an Nd:YAG pulsed laser) or by thermal desorption/electron capture. For each sample, a few micrograms of solid were loaded onto a stainless steel probe tip for examination. For the laser desorption experiments, the fourth harmonic of the YAG (266 nm) was used at 10^6 to 10^7 W/cm² to desorb and simultaneously ionize the fullerenes (37). Single laser shots of the "as is" samples generated ions that were trapped for between 3 and 20 ms at a base pressure of 8×10^{-9} Torr and subsequently detected in the FTMS ion cell. Both positive and negative ions were generated and examined in these studies. For the thermal desorption experiments, the probe tip containing the sample was heated slowly from 30° to 350°C to thermally desorb compounds from the sample. These neutral molecules were then ionized by low-energy electron capture to generate characteristic negative ions that could be monitored and compared to the laser desorption spectra.

25. M. V. Buchanan and M. B. Comisarov, in *Fourier Transform Mass Spectrometry: Evaluation, Innovation, and Application*, M. V. Buchanan, Eds. (American Chemical Society, 1987), pp. 1–19.

26. A. G. Marshal and P. B. Grosshans, *Anal. Chem.* 63, 215 (1991).

27. S. W. McElvany et al., *Chem. Phys. Lett.* 134, 214 (1987).

28. R. D. Knight et al., *Chem. Phys. Lett.* 129, 331 (1986).

29. P. F. Greenwood et al., *Fuel* 69, 257 (1990).

30. P. F. Greenwood, M. G. Strachan, G. D. Willett, M. A. Wilson, *Org. Mass Spec.* 25, 353 (1990).

31. P. F. Greenwood et al., *Org. Mass Spec.* 26, 920 (1991).

32. I. G. Dance, K. J. Fisher, G. D. Willet, M. A. Wilson, *J. Phys. Chem.* 95, 8425 (1991).

33. M. A. Wilson et al., *Nature* 356, 117 (1992).

34. D. M. Cox et al., *J. Amer. Chem. Soc.* 113, 2940 (1991).

35. C. S. Yoo and W. J. Nellis, *Science* 254, 1489 (1991).

36. J. E. Fisher et al., *ibid.* 252, 1288 (1991).

37. R. L. Hettich, R. N. Compton, R. H. Ritchie, *Phys. Rev. Lett.* 67, 1242 (1991).

38. We thank S. O. Firsova for providing shungite samples, data, and reprints; R. Dott for loan of a Precambrian anthracite sample from northern Michigan; J. Lehman for help with mass spectrometry at Arizona State University; T. Daly, W. Schopf, S. Wang, and P. Williams for valuable suggestions; N. Bostick for reprints; and T. Daly for helpful reviews. Electron microscopy was performed at the Facility for High Resolution Electron Microscopy at Arizona State University (ASU), which is supported by the National Science Foundation (NSF) and ASU. This study was supported by NSF grant EAR-870529 and private donors.

15 June 1992; accepted 19 June 1992

Programmed Death of T Cells in HIV-1 Infection

Linde Meyaard, Sigrid A. Otto, Richard R. Jonker, M. Janneke Mijnster, René P. M. Keet, Frank Miedema*

In human immunodeficiency virus (HIV) infection, functional defects and deletion of antigen-reactive T cells are more frequent than can be explained by direct viral infection. On culturing, both CD4⁺ and CD8⁺ T cells from asymptomatic HIV-infected individuals died as a result of programmed cell death (apoptosis). Apoptosis was enhanced by activation with CD3 antibodies. Programmed cell death, associated with impaired T cell reactivity, may thus be responsible for the deletion of reactive T cells that contributes to HIV-induced immunodeficiency.

Early in HIV infection, abnormalities in the immune system can be demonstrated in clinically stable asymptomatic individuals. HIV infection affects such $CD4^+$ and $CD8^+$ T cell functions as interleukin-2 production and proliferation after stimulation with soluble antigens and CD3 antibodies. These changes occur before $CD4^+$ T cell numbers are decreased (*1–5*) and cannot be attributed to direct HIV infection in vivo because only a relatively small number of T cells are infected (*6, 7*). In addition to deletion of T memory cells, intrinsic nonresponsiveness occurs in both $CD4^+$ and $CD8^+$ cells in long-term infections (*3, 4, 8*). In their nonresponsiveness to antigenic stimulation and lack of interleukin-2 production despite intact cell-signaling pathways (*1–4*), T cells in HIV-infected individuals exhibit the properties of the unresponsive state known as anergy (*9*).

$CD8^+$ T cells from HIV-infected individuals have increased expression of such activation markers as CD38, HLA-DR, and CD57, which suggests that there is continuous immune activation (*10, 11*). $CD8^+$ cells expressing activation markers have severely decreased proliferative responses and clonogenic potential (*12*) and are reported to die in culture (*13*). This suggests hyporesponsiveness in $CD8^+$ cells as a result of hyperactivation.

We considered the possibility that in this apparent anergic or hyperactivated state, T cells could be programmed for death and whether the loss of antigen-reactive cells could occur as a result of apoptosis. Programmed cell death (PCD), also known as apoptosis or activation-induced cell death, is a physiological mechanism of cell deletion that differs morphologically and biochemically from necrosis (*14*). PCD is involved in a wide variety of immunological regulatory processes (*14–16*). The process is characterized by a typical cellular morphology and degradation of the chromatin into discrete fragments that are multiples of about 190 base pairs of DNA (*17*). It has been proposed that in HIV infection interaction of soluble gp120 with CD4, previously shown to lead to impaired lymphocyte function (*18*), would prime $CD4^+$ T cells for PCD (*19*). This hypothesis is supported by results obtained with mature murine lymphocytes that die from PCD after stimulation through the T cell receptor complex when CD4 was previously ligated by CD4 antibodies (*20*).

Peripheral blood mononuclear cells (PBMC) from HIV-infected persons displayed morphology characteristic of PCD after being cultured overnight in the presence of antibodies to CD3 (anti-CD3) (Fig. 1). Cells showed extensive peripheral chromatin condensation, dilation of the endoplasmatic reticulum, and preservation of mitochondrial structures (*21*). To look for DNA fragmentation, we studied PBMC from 29 asymptomatic seropositive (CDC class II or III) homosexual men. They were selected from a prospective cohort study in Amsterdam (*22*) as having normal numbers of circulating $CD4^+$ cells (mean 540 per cubic millimeter, range 320 to 880) and being seropositive for longer than 3.5 years. In all experiments, a healthy male seronegative control was tested for each seropositive individual. All except one of the HIV-infected subjects showed decreased proliferative responses compared to the seronegative controls. Proliferation in response to anti-CD3 ranged from <1 to 80% of control values, as reported (*2–4, 8, 23*).

When low molecular weight DNA fractions were isolated from lysed cells and subjected to gel electrophoresis, the DNA cleavage pattern specific for apoptosis was observed. Fragmentation could be prevented by Zn^{2+}, which inhibits endonuclease activity (*24*) (Fig. 2). DNA fragments corresponding to 1 to 7 nucleosomes were identified by gel electrophoresis, but longer fragments were also detected that formed a smear in the gel near the origin of migration. In unstimulated cultures, DNA fragmentation was observed in

L. Meyaard, S. A. Otto, F. Miedema, Department of Clinical Viro-Immunology, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, and Laboratory for Experimental and Clinical Immunology of the University of Amsterdam, Plesmanlaan 125, 1066 CX Amsterdam, The Netherlands.
R. R. Jonker, Department of Molecular Pathology, TNO Institute of Applied Radiobiology and Immunology, Rijswijk, The Netherlands.
M. J. Mijnster, Netherlands Institute for Brain Research, Amsterdam, The Netherlands.
R. P. M. Keet, Department of Infectious Diseases, Municipal Health Service, Amsterdam, The Netherlands.

*To whom correspondence should be addressed.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
07/580,246	09/10/1990	DONALD R. HUFFMAN	7913Z	5441

7590 06/02/2005

SCULLY, SCOTT, MURPHY & PRESSER
400 GARDEN CITY PLAZA
GARDEN CITY, NY 11530

EXAMINER	
HENDRICKSON, STUART L	
ART UNIT	**PAPER NUMBER**
1754	

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 07/580,246
Filing Date: September 10, 1990
Appellant(s): HUFFMAN ET AL.

MAILED

JUN 03 2005

GROUP 1700

Mark J. Cohen
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 3/10/2005.

(1) ***Real Party in Interest***

A statement identifying the real party in interest is contained in the brief.

(2) ***Related Appeals and Interferences***

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Of note is that 08/236,933 has recently been decided.

(3) ***Status of Claims***

The statement of the status of the claims contained in the brief is correct.

(4) ***Status of Amendments After Final***

The appellant's statement of the status of amendments after final rejection contained in the brief is correct. **The amendment filed with the Brief has been entered.**

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct, noting that cancellation of claims has rendered moot the accompanying rejections thereof.

(7) Grouping of Claims

The rejection of claims on appeal stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is substantially correct. It appears in claim 156 that 'thin' has been changed to 'than'.

(9) Prior Art of Record

Kroto et al., NATURE volume 318 pg. 162 11/14/1985

Curl et al., SCIENTIFIC AMERICAN pg. 54 October 1991

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 53-72, 86, 96, 102-107, 111-114, 119, 122-132, 141-152, 154-157, 162, 165-170 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The substance of the rejection is set forth in the paper mailed 11/30/93.

Claims 53-73, 75, 80, 81, 86, 92, 93, 96, 102-107, 111-114, 119, 122-132, 141-157, 162, 165-170 are rejected under 35 U.S.C. 101.

The substance of this rejection is set forth in a prior Office Action, mailed on 11/30/93.

Claims 73, 75, 80, 81, 84, 89, 92, 93 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kroto et al. article in view of Curl et al. to show a state of fact.

The substance of this rejection is set forth in a prior Office Action, mailed on 11/30/93, noting that the claims reciting 'macroscopic' amounts are not rejected.

(11) Response to Argument

At the outset, it is noted that claim 156 may intend to refer to 'thin' layer chromatography and that the examiner will permit change thereto in a further amendment, in so far as this is necessary. With the Brief, appellants have file papers concerning proceedings of other applications, containing discussion of the term 'macroscopic'. These discussions are incorporated herein by reference.

For the reasons referred to in the above noted applications and papers, the term 'macroscopic' is deemed to lack support, despite the use of this term by independent authors to characterize the original NATURE article and the product made therein. The Declarations stating otherwise are opinion and hence are not persuasive. Merely because a material gives a colored solution does not mean that it is in amount which is a visible solid or macroscopic or crystalline. That the product gives an indicator which is visible does not mean that the material itself is visible. As an analogy, the turning of a pH indicator from clear to red does not mean that the protons themselves are visible. What Curl discusses does not make the present use of

'macroscopic' supported; if anything, the inability of Curl to make a macroscopic material confirms that this is not supported.

Concerning the 101 rejection, it stands to reason that a macroscopic amount of fullerenes are made by a wood-fueled fire, given that flames- particularly from aromatics- are sooty and are black with particulates. Given what is argued by appellant throughout, especially at Brief pg. 31, visible is equated to macroscopic. Terms such as 'formed' and 'molded' does not confer patentable distinction on the materials; one generally does not know the past history of a blob of material.

Kroto does not reject claims which recite 'macroscopic' amounts, thus rendering moot many arguments. Essentially, claims are rejected as being not supported due to the term 'macroscopic' or they are rejected over art if they lack the term 'macroscopic'. There is no inconsistency.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

STUART L. HENDRICKSON
PRIMARY EXAMINER

SLH
May 31, 2005

Conferees
Tom Dunn - SPE - AU1725
M. Nguyen SPE AU 1754

SCULLY, SCOTT, MURPHY & PRESSER
400 GARDEN CITY PLAZA
GARDEN CITY, NY 11530

Characterization of Carbonaceous Soots by Field Ionization Mass Spectrometry: In Search of C_{60} and Other Fullerenes

Ripudaman Malhotra* and David S. Ross

Chemistry Laboratory, SRI International, Menlo Park, California 94025-3493 *(Received: April 9, 1991)*

Characterization of several carbonaceous soots from pyrolysis and combustion processes by field ionization mass spectrometry shows the absence of peaks at 720 and 840 Da corresponding to C_{60} and C_{70} fullerenes. This absence coupled with the fact that these peaks are clearly seen in the soot obtained by vaporizing graphite in ~150 Torr of He leads to the conclusion that the commonly encountered pyrolysis and combustion soots do not contain significant (larger than 0.1%) amounts of fullerenes.

Introduction

Fullerenes are a recently discovered allotropic form of carbon consisting of cage structures. Their existence was first postulated by Osawa and Yoshida[1] in 1970, and the first evidence for their existence was obtained in laser desorption mass spectrometric studies by Kroto, Smalley, and co-workers[2] in 1985. Many reports have since appeared arguing for their abundant existence in nature in interstellar carbon clouds and in terrestrial soots formed during combustion of hydrocarbons.[3-5] The interstellar absorption at 217 nm, in particular, was attributed to fullerene species.[3] The presence of C_{60} and other nonplanar networks of sp^2 carbon in combustion soots was postulated on the basis that in relatively small carbon clusters planar graphitic sheets would be less stable because of unsatisfied valencies at the edges, and there would be a greater tendency in these structures to curl and ultimately form fullerene structures.

Recently, Krätschmer and Huffman reported the formation of fullerenes in bulk quantities by evaporating graphite in ~150 Torr of He.[6] This discovery presents an opportunity to measure the properties of fullerenes and develop unequivocal analytical tests to look for their presence in nature. Indeed, on the basis of the measured ultraviolet absorption spectrum, Huffman concluded that the 217-nm band cannot be due to fullerenes.[7] DeVries and co-workers have analyzed carbonaceous chondrites—Murchison and Allende meteorites—using photoionization mass spectrometry (PIMS) and also not found evidence for fullerenes.[8] Tingle et al. had also analyzed these chondrites using field ionization mass spectrometry (FIMS), as well as PIMS, and not found evidence for fullerenes.[9] However, because fullerenes were not the focus of that study, the conditions of analysis were not optimized for their detection. Ebert has questioned the hypothesis of soot beam composed predominantly of carbon clusters.[10] Using data from microanalysis, X-ray diffraction, and chemical reactivity of a diesel soot toward reductive alkylation, he concluded that soot consists of large planar aromatic molecules rather than carbon clusters. In this paper we provide direct evidence that C_{60} and related fullerenes are not present in the common carbonaceous soots formed during pyrolysis and combustion of hydrocarbons.

Experimental Section

Soot samples were collected from several sources: (1) vaporizing carbon in an arc in ~150 Torr of He,[11] (2) butane flame, (3) pyrolysis of butane at 1300 °C,[12] (4) diesel engine exhaust,[13] and (5) detonation of an RDX–TNT composite.[14] The soot samples were analyzed using FIMS by gradually heating them to 700 °C in the direct insertion probe of the mass spectrometer while continually recording the spectra of the evolved volatiles. Field ionization is a very gentle form of ionization and results in the formation of the molecular ion only for most organic compounds. The spectrometer used in this study consists of an activated-foil ionizer interfaced with a 60° magnetic sector mass analyzer.

Results and Discussion

Figure 1 shows the FI mass spectrum obtained by heating the soot derived from vaporizing graphite in ~150 Torr of He. The peaks due to C_{60} and C_{70} fullerenes are the dominant features in this spectrum. The peaks at m/z 720 and 840 are associated with peaks corresponding to natural abundance ^{13}C in the right proportions. Small peaks due to C_{76}, C_{78}, and C_{84} are also present. The small peaks at m/z 360 and 420 are due to doubly charged C_{60} and C_{70} fullerenes and not due to clusters of C_{30} and C_{35} because the coevolve with the peaks at 720 and 840.

In contrast to the spectrum of vaporized graphite, the spectra for all other carbonaceous soots (Figures 2 and 3) do not show any significant intensity at m/z 720 or 840.[15] The combustion soots were heated to above 700 °C, but the butane pyrolysis soot was heated only to 450 °C. While most of the C_{60} and C_{70} fullerenes vaporize in the inlet of the mass spectrometer in the 500–700 °C range, about 10% of the total peak intensity at m/z 720 and 840 evolves by 450 °C. Therefore, the complete absence

(1) (a) Osawa, E. *Kagaku (Kyoto)* 1970, *25*, 854. (b) Yoshida, Z.; Osawa, E. *Aromaticity*; Kgakudojin: Kyoto, 1971.

(2) Kroto, H. W., Heath, J. R.; O'Brien, S. C.; Curl, R. F.; Smalley, R. E. *Nature* 1985, *318*, 162–163.

(3) Kroto, H. W. *Science* 1988, *242*, 1139–1145.

(4) Zhang, Q. L.; O'Brien, S. C.; Heath, J. R.; Liu, Y.; Curl, R. F.; Kroto, H. W.; Smalley, R. E. *J. Phys. Chem.* 1986, *90*, 525–528.

(5) Kroto, H. W.; Heath, J. R.; O'Brien, S. C.; Curl, R. F.; Smalley, R. E. *Astrophys. J.* 1987, *314*, 352–355.

(6) Krätschner, W.; Fostiropoulos, K.; Huffman, D. R. *Chem. Phys. Lett.* 1990, *170*, 167–170.

(7) Krätschner, W.; Lamb, L. D.; Fostiropoulos, K.; Huffman, D. R. *Nature* 1990, *347*, 354–358.

(8) De Vries, M. S.; Wendt, H. R.; Hunziker, H.; Peterson, E.; Chang, S. Search of High Molecular Weight Polycyclic Aromatic Hydrocarbons and Fullerenes in Carbonaceous Meteorites. In *Proceedings of the 22nd Lunar and Planetary Science Conference*; Lunar and Platenary Institute: Houston, TX, 1991; pp 315–316.

(9) Tingle, T. N.; Becker, C. H.; Malhotra, R. Organic Compounds in the Murchison and Allende Carbonaceous Chondrites Studied by Photoionization and Field Ionization Mass Spectrometry. *Meteoritics*, accepted for publication.

(10) Ebert, L. B. *Science* 1990, *247*, 1468–1471.

(11) Bae, Y. K.; Lorents, D. L.; Malhotra, R.; Becker, C. H.; Tse, D. S.; Jusinsky, L. Production, Characterization, and Deposition of Carbon Clusters. In *Proceedings of the MRS Society Meeting on Clusters and Cluster-Assembled Materials*; *Baston, MA, 1990*.

(12) Solomon, P. R.; Hamblen, D. G.; Serio, M. A.; Tarantul, K. S.; Markham, J. R. Experiments and Modeling of Multi-Component Combustion. Final Report for U.S. Air Force, Air Force Wright Aeronautical Laboratories, AFWAL-TR-87-2097, March 1988.

(13) Diesel Particulate Matter, NIST Ref No. 1650.

(14) (a) Greiner, R. N.; Phillips, D. S.; Johnson, J. D.; Volk, F. *Nature* 1988, *333*, 440–442. (b) Greiner, R. N.; Hermes, R. Chemistry of Detonation Soot: Diamonds, Graphite, and Volatiles. In *Proceedings of the 9th Symposium (Intl.) on Detonation, Portland, OR, 1989*; pp 522–527.

(15) The spectra in Figures 2 and 3 were recorded several years ago. At that time we could not make a categorical statement regarding the absence of fullerenes for we were not sure whether they would be sufficiently volatile to be detected by FIMS.

0022-3654/91/2095-4599$02.50/0

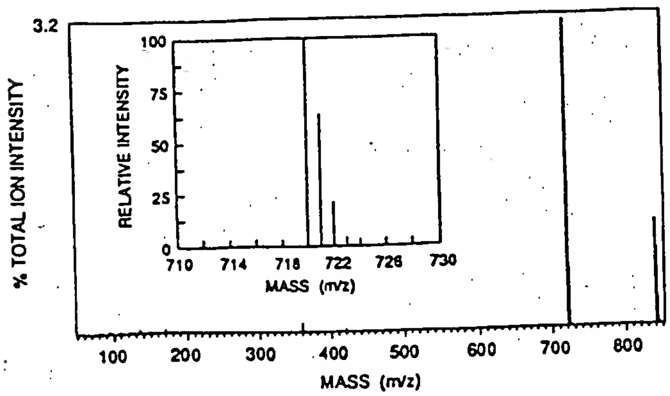

Figure 1. Field ionization mass spectrum of soot obtained by vaporizing graphite shows peaks due to C_{60} and C_{70}. Inset: expanded region around mass 720 showing the isotopic satellites.

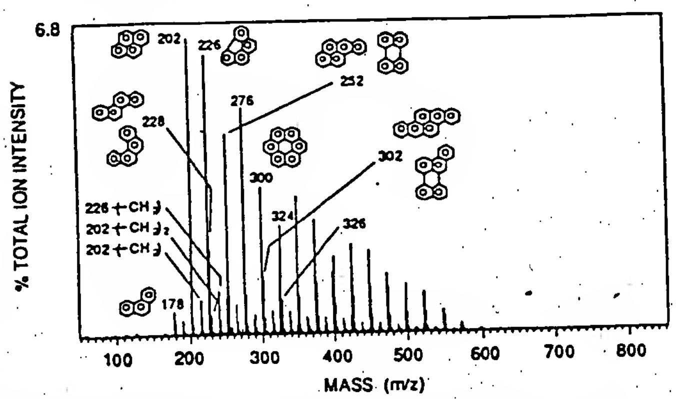

Figure 2. Field ionization mass spectrum of soot from pyrolysis of butane showing the sequence of PCAH intermediates and their alkylated derivatives. (Sample courtesy of Dr. P. R. Solomon.)

of peaks at 720 and 840 Da rules out the presence of C_{60} and C_{70} fullerenes also in the pyrolysis soot. What Figures 2 and 3 show instead are series of peaks in the 100–400-Da range, many of which can be attributed to polycyclic aromatic hydrocarbons (PCAH).

Several studies have shown that extraction of soots with refluxing solvents can yield considerable quantities of PCAH;[16,17] however, because of the limited solubility of many of the PCAH, the extracts rarely show the presence of hydrocarbons larger than coronene. It is notable that, in contrast to the case for extraction, greater than 80% of the FIMS signal falls above 300 Da. The prominent peaks in the spectrum for butane pyrolysis soot correspond to chrysene, benzchrysene, dibenzchrysene, and so on, giving rise to a series of peaks separated by 50 Da. Another series of benzologues which differs from the chrysene series by 24 Da, pyrene, benzpyrene/perylene, and their benzologues, is also evident.

Also notable is the absence of the peak due to corannulene (m/z 250) from the spectra in Figures 2 and 3. We do not believe that we are discriminating against corannulene because the peak due to benzpyrene/perylene, only 2 mass units apart, is quite prominent. Corannulene, with its five-membered ring, provides the puckering necessary for the building of fullerene structures and is considered to be their precursor. Stein and Fahr[18] have calculated the stabilities of various PCAH structures and have noted that corannulene was considerably less stable than its isomer, which contains only six-membered rings. McKinnon has also calculated the potential yields of fullerenes in hydrocarbon combustion and pyrolysis from thermodynamic data.[19] According to him, full-

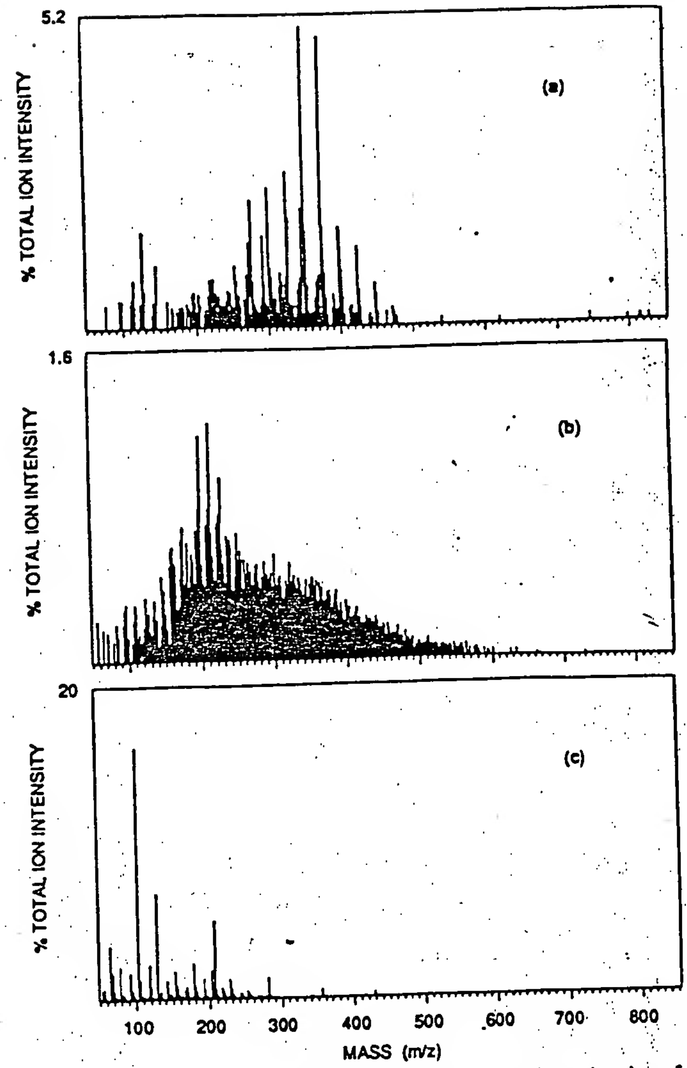

Figure 3. Field ionization mass spectra of soot from (a) combustion of butane (open flame), (b) diesel exhaust (NIST reference material), and (c), detonation of RDX–TNT composite. (Sample courtesy of Dr. R. Greiner.)

erenes could be produced only in a narrow temperature window around 2400 K and in the absence—or only very small amounts—of hydrogen and oxygen. Increase in the amount of hydrogen severely depresses the calculated yield. Of course, thermodynamics do not alone control the formation of fullerenes; kinetic factors also play an important role. On kinetic grounds, Frenklach and others have argued that soot formation during combustion and pyrolysis of hydrocarbons will not lead to fullerene structures.[20] They found that kinetic factors overwhelmingly favored growth via planar structures (*peri-condensed*) than bent structures (*peri- and cata-condensed*). FIMS data reported here provide direct evidence for this conclusion.

The FI mass spectra are largely, if not fully, the result of evaporation of preexisting compounds into the instrument, rather than pyrolytic fragmentation of larger structures on the soot surface. This conclusion is based on the fact that the number-average molecular weight ($\bar{M}_n$) of the volatiles increases monotonically with temperature up to the highest values. When thermal fragmentation is significant, as it is in coal tars for example, there

(16) Butler, J. D.; Crossley, P. *Atmos. Environ.* **1981**, *15*, 91–94.
(17) Prado, G. P.; Lee, M. L.; Hites, R. A.; Hoult, D. P.; Howard, J. B. Soot and Hydrocarbon Formation in a Turbulent Diffusion Flame. In *Proceedings of the 16th Symposium (International) on Combustion*; The Combustion Institute: Pittsburgh, PA, 1977; pp 649–661.
(19) (a) McKinnon, J. T. Calculated Equilibrium Yields of Buckminsterfullerene from Hydrocarbon Pyrolysis and Combustion. Submitted for publication in *J. Phys. Chem.* (b) McKinnon, J. T.; Bell W. Synthesis of Buckminsterfullerene in a Sooting Flame. In *Proceedings of the Western States Section of the Combustion Institute Spring Meeting, Boulder, CO, 1991*.
(20) (a) Frenklach, M.; Clary, D. W.; Gardiner, W. C., Jr.; Stein, S. E. *Combust. Sci. Technol.* 1986, *50*, 79–101. (b) Frenklach, M.; Ebert, L. B. ... 1988, 92, 561–563.

...falloff in $\bar{M}_n$ at 350–450 °C.[21] The sc...pectra ...ed here thus represent the volatile components (tar) present ...soot.

...e spectrum for the soot from a diesel engine (Figure 3b) ...s the presence of the unburnt fuel (m/z 150–250 range) ...imposed on a broader envelope of peaks at every mass up ...out 600 amu. Apparently, this soot was formed under the ...tions that do not defunctionalize the original hydrocarbon ...tures completely. In the case of the soot from the detonation ...DX–TNT composite (Figure 3c), we can find substantial ...sity of peaks at odd masses corresponding to nitrogen-con...ng compounds. Two series of prominent peaks are evident ...s spectrum: (i) due to benzonitrile (m/z 103) and its ben...gues at m/z 153 and 203 and (ii) due to naphthalene (m/z 128) and its benzologues at m/z 1... (phenanthrene) and 228. Weaker peaks due to alkylated homologues (e.g. at m/z 117 due to methylbenzonitrile) are present. In preliminary work, we have also examined soots from combustion of polymers such as polyurethane, polystyrene, and polyoxazoline. These soots give spectra with features characterized by oligomeric species but, again, no peaks corresponding to fullerenes were observed.

In summary, the lack of peaks due to C_{60} and C_{70} in the FI mass spectra of most of the common soots is in concert with the conclusion of Frenklach and Ebert[20b] that pyrolysis and combustion of organic materials does not generally lead to soots with fullerene structures.

Acknowledgment. We are grateful to Dr. L. Ebert for encouraging us to examine this question. We thank Dr. P. R. Solomon for the sample of the butane pyrolysis soot and Dr. R. Greiner for the soot from RDX–TNT detonation. This work was supported by SRI's IR&D Fund.

...1) Ross, D. S.; Hirschon, A. *Am. Chem. Soc., Div. Fuel Chem., Prepr.* 1990, *35*, 37–45.

...EATURE ARTICLE

...drogen Bonds as Design Elements in Organic Chemistry

Margaret C. Etter

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455 *(Received: October 2, 1990; In Final Form: December 26, 1990)*

This work involves the use of crystal chemistry and crystallographic data base analyses as a way to study hydrogen-bond directed molecular recognition properties of organic molecules. By using the solid phase rather than solution, our studies are not limited to tightly bound dimeric species but encompass aggregate structures with multiple molecules, intricate interlinked patterns, and both strong and weak (often *very* weak) intermolecular interactions. The point of view taken here is to analyze the consequences of directed and selective hydrogen-bond interactions on sets of molecules rather than focusing on the energy or geometry of individual hydrogen-bond interactions. The "consequences" are to a solid-state chemist what a new synthesis is to a solution chemist, i.e., the formation of new chemical species. Methods for deriving hydrogen-bond rules from large sets of crystal structures are presented here. Ways to prepare organic cocrystals and to use cocrystallization to probe the forces involved in aggregation phenomena are discussed, and examples are given of how molecular aggregation can impart unexpected new properties to organic compounds.

...valent bonds are the primary design elements in organic ...ules. They are stable enough to be detected and directional ...h to have predictable structural consequences and occur ...ntly enough to be of practical interest. Hydrogen bonds ... similar role in organic materials, yet they have escaped ...ts at systematization of this role; hence, their use as a tool ...rying out "intermolecular syntheses" has been nearly ne...d.[1] The products of these intermolecular syntheses are ...gen-bonded molecular aggregates, defined by connectivity ...ns arising from hydrogen bonds. These aggregates could ...n solution, at interfaces, or in the solid state.

...ently, considerable effort has been devoted to the study of ...lar association in solution, especially for cases where the ...ate pattern that is formed involves only two species (usually ...a host and a guest), where association or binding constants are very high (10^4 M^{-1} or greater) and where the aggregates are stabilized primarily by topological features such as preorganized cavities.[2] Such systems are important as small molecule models of enzyme activity. Our work addresses the general class of molecular aggregates, including species with weak association constants as well as species with multiple molecules per aggregate structure. Such species are extremely difficult to study in solution, but they are as easy to study in the solid state as are dimers with high solution binding constants. Our work has focused on the role of hydrogen bonds in the absence of preorganized cavities specifically so we could evaluate the independent contributions (such as selectivity or topology) of hydrogen-bonding groups to the structures of aggregates.

...(1) ...few notable exceptions include: (a) Ducharme, Y.; Wuest, J. D. *J. ...em.* 1988, *53*, 5789–5791. (b) Weber, E.; Hecker, M.; Csöregh, I. ...*Chem. Soc.* 1989, *111*, 7866–7872. (c) Hart, H.; Lin, L.-T. W.; Ward, ...*Am. Chem. Soc.* 1984, *106*, 4043–4045. (d) Zerkowski, J. A.; Seto, ...Vierda, D. A.; Whitesides, G. M. *J. Am. Chem. Soc.* 1990, *112*, ...126.

(2) (a) Rebek, J., Jr. *Angew. Chem.* 1990, *102*, 261. (b) Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* 1990, *112*, 7278–7286. (c) Diederich, F. *Angew. Chem., Int. Ed. Engl.* 1988, *27*, 362–386. (d) Friedrichsen, B. P.; Powell, D. R.; Whitlock, H. W. *J. Am. Chem. Soc.* 1990, *112*, 8931–8941. (e) Hamilton, A. D.; Pant, N.; Muehldorf, A. *Pure Appl. Chem.* 1988, *60*, 533–538. (f) Zimmerman, S. C.; Wu, W. *J. Am. Chem. Soc.* 1989, *111*, 8054–8055. (g) Kelly, T. R.; Maguire, M. P. *J. Am. Chem. Soc.* 1987, *109*, 6549–6551. (h) Bell, T. W.; Liu, J. *J. Am. Chem. Soc.* 1988, *110*, 3673–3674.

0022-3654/91/2095-4601$02.50/0